BIOGRAPHICAL SKETCH

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NAME: Liu, Liping

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POSITION TITLE: Postdoctoral Scholar

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Tsinghua University, Beijing, Beijing	BS	07/2002	Biological science
Medical University of South Carolina, Charleston, South Carolina	PHD	12/2020	Cell and Molecular Pharmacology
National Institute of Diabetes, Digestive and Kidney Diseases, Bethesda, Maryland	Other training	05/2015	Biochemistry and Cellular Biology
Medical University of South Carolin, Charleston, South Carolina	Other training	12/2021	Mass Spectrometry
Stanford University, Palo Alto, California	Postdoctoral Fellow	present	Neurodegenerative Disease

A. Personal Statement

I have more than 10 years academic training and research experience in multiple biological disciplines including biochemistry especially protein biology, cell and molecular pharmacology, and mass spectrometry. As undergraduate in Tsinghua University and predoctoral in Chinese Academy of Science, I have strong background on biophysics and biochemistry, and conducted research on protein expression and purification on various platforms, cloning and mutagenesis, artificial protein designation and analysis skills on protein structure. In the two and half years in Dr. Ye's lab in NIDDK, I was led into the interesting field of Endoplasmic-reticulum-associated protein degradation (ERAD), ER stress and unfolded protein response (UPR). After assisting Postdoc and iterating over projects including structure of E2, identification of novel E3 ligase and corporative chaperons, and the roles of USPs, I was well trained in the bench skills and more importantly I developed the panorama sketch of ERAD in my mind. In the Ph.D training in Dr.Mariana Pehar's lab in MUSC, I performed several projects focus on misfolded protein and ER stress in neurodegenerative disease . More importantly, based on our research on molecular mechanisms of astrocyte-mediated neurotoxicity in ALS, we evaluated the pharmaceutical potential of novel therapies targeting RAGE in ALS and unveiled its key role, as the first, in disease progression in a sex-dependent and a cell type/tissue-specific context. In Dr. Drake Richard lab in MUSC, I was trained in Mass Spectrometry and contributed to development a glycoproteomic method to selectively enrich 2,3 SA and 2,8 SA containing glycoprotein/peptide from human fluid sample, which could be indicator of various neurodegeneration. For my postdoctoral training, I will continue my perspiration in development the meaningful therapies treating Glaucoma under Dr.Yang Hu's direction, via integrating my previous experience on pharmacology and neurodegenerative disease. My sponsor Dr. Yang Hu is an internationally recognized leader in the Glaucoma research field and has a successful record of training postdoctoral fellows. The proposed research can provide me with new conceptual and technical training in drug development in ophthalmology. Additionally, the proposed training plan in Stanford brings a set of career development activities and workshops including grant writing, public lecture and lab management. Taken together, the training in Stanford will give me a solid foundation to reach my goal: becoming an successful researcher and developing the meaningful therapies to change the fate of patients suffering from neurodegenerative disease.

1. Blaschke CRK, Hartig JP, Grimsley G, Liu L, Semmes OJ, Wu JD, Ippolito JE, Hughes-Halbert C, Nyalwidhe JO, Drake RR. Direct N-Glycosylation Profiling of Urine and Prostatic Fluid Glycoproteins and Extracellular Vesicles. Front Chem. 2021;9:734280. PubMed Central PMCID: PMC8503230.
2. Liu L, Killoy KM, Vargas MR, Yamamoto Y, Pehar M. Effects of RAGE inhibition on the progression of the disease in hSOD1^{G93A} ALS mice. Pharmacol Res Perspect. 2020 Aug;8(4):e00636. PubMed Central PMCID: PMC7415959.
3. Harlan BA, Killoy KM, Pehar M, Liu L, Auwerx J, Vargas MR. Evaluation of the NAD^+ biosynthetic pathway in ALS patients and effect of modulating NAD^+ levels in hSOD1-linked ALS mouse models. Exp Neurol. 2020 May;327:113219. PubMed Central PMCID: PMC7089832.
4. Liu Y, Soetandyo N, Lee JG, Liu L, Xu Y, Clemons WM Jr, Ye Y. USP13 antagonizes gp78 to maintain functionality of a chaperone in ER-associated degradation. Elife. 2014;3:e01369. PubMed Central PMCID: PMC3889402.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2022 -	Postdoctoral Scholar, Stanford University, Palo Alto, CA
2020 - 2021	Research Specialist, Medical University of South Carolina, Charleston, SC
2015 - 2020	Graduate Research Assistant, Medical University of South Carolina, Charleston, SC
2012 - 2015	Research Specialist (Volunteer), NIDDK, Bethesda, MD

Honors

2021	Wiley Top Cited article 2020-2021, Wiley

C. Contribution to Science

1. Early Career: My main contributions in early scientific career were focused on employing my knowledge and experience of protein chemistry to exploring novel mechanisms in ERAD and UPR. More specifically, working in Dr.Ye's lab in NIH, I selected, purified, and prepared soluble misfolded proteins (splitted GFP etc.) and ensured the semi-quantification of affinity between cell membrane and misfolded proteins and therefore contribute to build a novel model to explore endocytosis of misfolded proteins. Also, I designed and produced soluble Lunapark, a new E3 ligase, by replacing its 2 transmembrane domains with optimized linkers and identified its enzyme activity. Moreover, I designed and purified a series of USP5/USP13 truncation mutants, and chimera proteins for enzyme assays and interactome research.

    a. Liu Y, Soetandyo N, Lee JG, Liu L, Xu Y, Clemons WM Jr, Ye Y. USP13 antagonizes gp78 to maintain functionality of a chaperone in ER-associated degradation. Elife. 2014;3:e01369. PubMed Central PMCID: PMC3889402.

2. Graduate Career: My graduate research contributions focused on misfolded protein and ER stress in cancer and neurodegenerative disease. Results from my research provided new details into pathological mechanisms involved in ALS disease progression and advanced development of pharmaceutical drugs to treat this deadly disease without any efficient therapy. More specifically, I successfully created and optimized the first mammalian cell-based platform able to express and purify natural soluble mutants of neurotrophic growth factors, which removed the biggest stumbling block on the path, and address the key role of PTM of neurotrophic growth factors in pathology of neurodegenerative disorders like ALS. I developed in vitro drug screen platforms (Magnetic and FRET) to identify novel antagonists of RAGE/P75NTR. I analyzed the effects of pharmaceutical drugs on primary astrocytes, and identified alternation of inflammation, metabolism and secretion in astrocytes and explore the relative mechanism responsible for neuroprotective/neurotoxic effects of RAGE signaling in astrocyte. Moreover, I evaluated the effects of pharmaceutical inhibitor and gene

depletion on ALS mouse model. By continuous daily research as long as 950 days, I successfully addressed the sex dependent and phase dependent neuroprotective/neurotoxic effects of RAGE inhibition via pharmaceuticals and gene depletion in ALS mice. Furthermore, we pointed out the positive effect on skeleton muscle atrophy while negative effect on inflammation and fibrosis in lung. Subsequently new target and approach of therapy were addressed for future research. Based on my research, evaluation of new therapy to treat ALS with known drugs was in progress in our collaborative lab.

a. Liu L, Killoy KM, Vargas MR, Yamamoto Y, Pehar M. Effects of RAGE inhibition on the progression of the disease in hSOD1^{G93A} ALS mice. Pharmacol Res Perspect. 2020 Aug;8(4):e00636. PubMed Central PMCID: PMC7415959.
b. Harlan BA, Killoy KM, Pehar M, Liu L, Auwerx J, Vargas MR. Evaluation of the NAD^+ biosynthetic pathway in ALS patients and effect of modulating NAD^+ levels in hSOD1-linked ALS mouse models. Exp Neurol. 2020 May;327:113219. PubMed Central PMCID: PMC7089832.

3. Postdoctoral Career:I involved into successful development of a glycoproteomic identification method, named SABER (Sialic Acid Beads Enrichment Reaction) to selectively enrich 2,3 SA and 2,8 SA containing glycoprotein/peptide from human fluid sample (serum, plasma and urine). I made the key contribution to create, troubleshoot and optimize the novel protocols of abundant protein depletion, target protein enrichment in serum and hence significantly increase efficiency and specificity of targeted protein enrichment. I was responsible for performing experiments to answer critical questions from funding reviewers and integrated SOPs to meet request of collaborators. Project successfully got NIH fund in 2022

a. Blaschke CRK, Hartig JP, Grimsley G, Liu L, Semmes OJ, Wu JD, Ippolito JE, Hughes-Halbert C, Nyalwidhe JO, Drake RR. Direct N-Glycosylation Profiling of Urine and Prostatic Fluid Glycoproteins and Extracellular Vesicles. Front Chem. 2021;9:734280. PubMed Central PMCID: PMC8503230.